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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/707,892	11/06/2000	Robert H. Austin	4555-107 US	9832

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EXAMINER

BROWN, JENNINE M

ART UNIT

PAPER NUMBER

1743

DATE MAILED: 07/31/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/707,892	AUSTIN ET AL.
	Examiner	Art Unit
	Jennine M. Brown	1743

— The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on _____.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-23 is/are pending in the application.
 - 4a) Of the above claim(s) 24-32 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-23 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All
 - b) Some *
 - c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 - a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____.
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>6</u> .	6) <input type="checkbox"/> Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 6 recites the limitation "applied frequency" in line 24 of page 35. There is insufficient antecedent basis for this limitation in the claim. It would be appropriate to change the term to "predetermined frequency".

Claims 5 and 7 recite the limitation "said electrical signal" in line 21 and 27 respectively on page 35. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (e) the invention was described in–
 - (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
 - (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 1-2, 4, 8, 10, 13, 15-18 are rejected under 35 U.S.C. 102(e) as being anticipated by Regnier, et al. (US 6156273).

Regarding claim 1, Regnier, et al. teach a microfluidic device with a plurality of constrictions (14) separated from one another by a gap (12, 104) and a means for passing polarizable particles in the vicinity of the constrictions by applying a dielectrophoretic field (Figure 4A) to trap particles in the gap (Figures 1A-8; col. 2, l. 1-62; col. 4, l. 61 – col. 5, l. 7; col. 5, l. 37-55; col. 12, l. 53 – col. 16, l. 65).

Regarding claim 2, Regnier, et al. teach a fluid input means for inputting fluid (col. 2, l. 29-35).

Regarding claim 4, Regnier, et al. teach an electrical signal applied to a pair of electrodes on opposite edges of substrate (col. 9, l. 61-67).

Regarding claim 8, Regnier, et al. teach that the constrictions are formed on a substrate using a photolithographic etch (abstract; col. 4, l. 26 – col. 5, l. 36).

Regarding claim 10, Regnier, et al. teach that the distance between constrictions is not to exceed 10 to 100 micrometers (col. 4, l. 5-10; col. 7, l. 21-23).

Regarding claim 13, Regnier et al. teach a distance between rows of constrictions having varied geometric shapes and those rows can be equally spaced or differently spaced as shown in Figures 1A-6.

Regarding claim 15, Regnier, et al teach that the substrate can be quartz and silicon (col. 4, l. 49-51).

Regarding claim 16, Regnier, et al. teach that there is a cover plate (13) used which is sealed to the substrate (col. 5, l. 8-23).

Regarding claims 17-18, Regnier, et al. teach through Figure 1A an area of tightly placed constrictions (top of drawing) next to fewer more widely spaced constrictions (branches towards middle of drawing) to even further spaced apart constrictions (branches towards bottom left hand side of drawing).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 3, 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Regnier, et al. (US 6156273) in view of Kopf-Sill, et al. (US 6358387).

Regnier, et al. teach a microfluidic device as described above.

Regarding claim 3, Regnier, et al. do not specifically teach the use of a syringe pump for pressure driven fluid input means (col. 4, l. 11-25; col. 5, l. 40-41). Kopf-Sill,

et al. teach a microfluidic device with both electrochemical and pressure (syringe pump) movement of fluids on the microfluidic device (col. 15, l. 37 – col. 16, l. 14).

It would have been obvious to one of ordinary skill in the art to modify the device of Regnier, et al. to include the syringe pump method of fluid movement as described by Kopf-Sill, et al. because both are micromachined microfluidic devices used for electrophoresis and it would have been obvious to include either electrical, mechanical or a combination of both means to move fluids within the microchannels as stated in the disclosure of Kopf-Sill, et al.

Regarding claim 23, Regnier, et al. do not specifically teach the heating means adjacent said constrictions. Kopf-Sill, et al. teach the use of heating means adjacent to the channels in a microfluidic chip which uses electrofocusing of analytes (col. 9, l. 36 – col. 10, l. 20).

It would have been obvious to one of ordinary skill in the art to add the heating block layer element of Kopf-Sill, et al. to the apparatus of Regnier, et al. because it would aid in heating or cooling of separated materials for further denaturing, chelating or other reactions where heating or cooling is required so that labeling agents or taggants can be added to a biochemical analyte in order to detect fluorescence in the material.

Claims 5-7, 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Regnier, et al. (US 6156273) in view of Walters, et al. (US 6117660).

Regnier, et al. teach a microfluidic device as described above.

Regarding claims 5-7, Regnier, et al. do not specifically teach AC voltages at a predetermined frequency or DC voltage. Walters, et al. teach AC or DC voltage at a predetermined frequency for dielectrophoresis (col. 1, l. 49-52) specifically the range of 1Hz (col. 2, l. 39-48; col. 3, l. 23-24; col. 4, l. 7-10, 44-48; col. 5, l. 64-65; col. 6, l. 15-16, 26-28, 34-35; col. 7, l. 13-16, 19-21; col. 10, l. 27-37).

It would have been obvious to one of ordinary skill in the art to use the predetermined AC voltage frequency of Walters, et al. in the apparatus of Regnier, et al. because it will provide for dielectric pumping of analyte in an electrophoretic apparatus where low temperatures are required and where the coating on the monolithic structures acts similarly to a treated membrane which is used in the electroportation and electrofusion art.

Regarding claim 9, Regnier, et al. teach using coating moieties of anionic groups, cationic groups, antibodies, antigens and chelation groups which are used to bind things like ssDNA, dsDNA, RNA, cells and polymer particles but do not specifically address biological polymers as the particles being separated. Walters, et al. teach that apparatus for electromanipulation (i.e. electrophoresis) is used on DNA material (col. 2, l. 67), cell membranes (col. 2, l. 6-7) and other materials as discussed in the background of the art (col. 1, l. 13 - col. 10, l. 37). It would have been obvious to one having ordinary skill in the art to specifically separate biological polymers with the

device of Regnier, et al. because biological polymers are specifically responsive to electrophoresis.

Claims 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Regnier, et al. (US 6156273) in view of Austin, et al. (US 5427663).

Regnier, et al. teach a microfluidic device as described above.

Regarding claim 11, Regnier, et al. do not specifically teach the height between 0.5 to 5 micrometers. Austin, et al. teach a microfluidic device with the same types of constrictions used by Regnier, et al. where the height range is between 0.01 and 20.0 micrometers.

It would have been obvious to one of ordinary skill in the art to modify the apparatus of Regnier, et al. to decrease the height of the apparatus as is stated by Austin, et al. so that the obstacles had a height between 0.01 and 20.0 micrometers because this would constrict the separating mixture to one layer of cells, particles or other analyte to be separated.

Regarding claim 12, Regnier, et al. state that the preferred distance between the constrictions is 1 micrometer and it would have been obvious to one of ordinary skill in the art to using the reasoning stated regarding claim 11 that the height would need to be large enough to reduce the amount of Joule heating while being small enough to allow only particles of analytes like RNA and DNA to be separated out.

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Regnier, et al. (US 6156273) or Austin, et al. (US 5427663).

Regnier, et al. teach a microfluidic device as described above.

Regnier, et al. do not specifically teach a trapezoidal shape for the constrictions, but it would have been obvious for one of ordinary skill in the art to change the shape of the constriction. Austin, et al. also teach different shapes for constrictions (col. 20, l. 41-44) although trapezoidal shaped is not specifically shown, the arrow shaped constrictions shown in Figure 7 resemble a trapezoidal shape enough that it would have been obvious to one of ordinary skill in the art to substitute a shape change for the constriction because it can easily be changed during the lithography of the substrate. Also the disclosure does not state any specific advantage that the trapezoidal shape gives over all shapes shown for the configurations in both Regnier, et al. and Austin, et al.

Claims 19-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Regnier, et al. (US 6156273) in view of Quake, et al. (US 6344325).

Regnier, et al. teach a microfluidic device as described above.

Regarding claim 19, Regnier, et al. do not specifically teach one or more channels coupled to the end of the regions for extracting polarizable particles. Quake, et al. teach a microfluidic device having one or more channels coupled to the end of regions for extracting polarizable particles (Figures 1-7; col. 2, l. 39 -56).

It would have been obvious to one of ordinary skill in the art to combine the channels of Quake, et al. with the constriction based microfluidic apparatus of Regnier, et al. because the channels will give the user the ability to provide further analysis on the fractionated species from the constrictions.

Regarding claim 20, Regnier, et al. do not specifically teach a matrix in a channel downstream from the constrictions capable of fractioning and/or analyzing the particles. Quake, et al. teach fractioning and analyzing the particles separated (col. 2, l. 57 – col. 5, l. 46).

It would have been obvious to one of ordinary skill in the art to combine the channels of Quake, et al. with the constriction based microfluidic apparatus of Regnier, et al. because the channels will give the user the ability to provide further analysis on the fractionated species from the constrictions because each constriction would be identified by another means such as fluorescent imaging.

Regarding claim 21, Regnier, et al. do not specifically teach imaging equipment to visualize the polarizable particles. Quake, et al. teach fluorescent imaging of separated particles (col. 2, l. 57 – col. 5, l. 46).

It would have been obvious to one of ordinary skill in the art to combine the channels of Quake, et al. with the constriction based microfluidic apparatus of Regnier, et al. because the channels will give the user the ability to provide further analysis on the fractionated species from the constrictions because each constriction would be identified by another means such as fluorescent imaging.

Regarding claim 22, Regnier, et al. teach siloxane substrates as explained previously but do not specifically teach substrate material of polyimide, PDMS or PMMA. Quake, et al. teach PMMA as a substrate resist material deposited on the surface of the substrate.

It would have been obvious to one of ordinary skill in the art to use PMMA photoresist as the etchant material for the substrate because it would have the hydrophobicity required for certain types of wall materials created for the channels of the substrate and is easier to control and cheaper to use than traditional wet etching methods.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennine M. Brown whose telephone number is (703) 305-0435. The examiner can normally be reached on M-F 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (703) 308-4037. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 879-9310 for regular communications and (703) 872-9311 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.

jmb
July 29, 2002


Jill Warden
Supervisory Patent Examiner
Technology Center 1700